

CLAIMS

What is claimed is:

- 1 1. A method of therapy for a mammal at risk of, or afflicted with, loss of or damage to
2 myocardium, the method comprising
3 implanting a preparation of myogenic precursor cells into said mammal at a site at risk of,
4 or afflicted with, loss of or damage to myocardium, and
5 treating said myogenic precursor cells with an amount of a morphogen sufficient to
6 promote proliferation or differentiation of said myogenic precursor cells into functional
7 myocardium.
- 1 2. A method of therapy for a mammal at risk of, or afflicted with, loss of or damage to
2 myocardium, the method comprising
3 implanting a preparation of myogenic precursor cells into said mammal at a site at risk of,
4 or afflicted with, loss of or damage to myocardium, and
5 treating said mammal with an amount of an inducer of a morphogen encoded by a gene of
6 said mammal, said amount being sufficient to promote proliferation or differentiation of said
7 myogenic precursor cells into functional myocardium.
- 1 3. A method of therapy for a mammal at risk of, or afflicted with, loss of or damage to
2 myocardium, the method comprising
3 implanting a preparation of myogenic precursor cells into said mammal at a site at risk of,
4 or afflicted with, loss of or damage to myocardium, and
5 treating said myogenic precursor cells with an amount of an agonist of a morphogen
6 receptor expressed by said myogenic precursor cells, said amount being sufficient to promote
7 proliferation or differentiation of said myogenic precursor cells into functional myocardium.
- 1 4. A method of therapy for a mammal at risk of, or afflicted with, loss of or damage to
2 myocardium, the method comprising
3 implanting a preparation of myogenic precursor cells into said mammal at a site at risk of,
4 or afflicted with, loss of or damage to myocardium, and

5 treating said myogenic precursor cells with an amount of a small molecule morphogenic
6 activator, said amount being sufficient to promote proliferation or differentiation of said myogenic
7 precursor cells into functional myocardium.

1 5. A method as in any one of claims 1-4 wherein said myogenic precursor cells are selected
2 from the group consisting of mammalian skeletal muscle satellite cells, embryonic myogenic
3 precursor cells, and a histocompatible mammalian myogenic precursor cell line.

1 6. A method as in any one of claims 1-4 wherein said myogenic precursor cells are
2 autologous skeletal muscle satellite cells.

1 7. A method as in any one of claims 1-4 wherein
2 said mammal is afflicted with a condition selected from the group consisting of myocardial
3 infarction and congestive heart failure.

1 8. A method as in any one of claims 1-4 wherein said treatment step is conducted prior to
2 said implantation step.

1 9. A method as in any one of claims 1-4 wherein said treatment step is conducted
2 simultaneous with said implantation step.

1 10. A method as in any one of claims 1-4 wherein said treatment step is conducted subsequent
2 to said implantation step.

1 11. A method as in claim 10 wherein said treatment step is at least once a week for a period of
2 at least four weeks.

1 12. A method as in claim 10 wherein said treatment step is at least once a month for a period
2 of at least one year.

1 13. A method as in claim 1 wherein said morphogen treatment step is conducted with
2 morphogen at a concentration of about 0.01-1000 ng/ml.

1 14. A method as in claim 1 wherein said morphogen treatment step is conducted with
2 morphogen at a concentration of about 0.1-100 ng/ml.

1 15. A method of promoting proliferation of myogenic precursor cells or differentiation of
2 myogenic precursor cells into functional myocardium comprising the steps of:

3 (a) contacting said cells with a morphogen in an amount effective to induce said
4 proliferation or differentiation; and

5 (b) maintaining said cells in a morphogenically permissive environment.

1 16. A method as in claim 1 wherein said morphogen is selected from the group consisting of a
2 pro form of a morphogen, a soluble form of a morphogen, a mature morphogen, and a C-terminal
3 fragment of a morphogen comprising at least the seven cysteine domain of said morphogen.

1 17. A method as in claim 1 wherein said morphogen is selected from the group consisting of
2 osteogenic proteins and bone morphogenic proteins.

1 18. A method as in claim 1 wherein said morphogen
2 induces a cascade of tissue-specific morphogenesis culminating in the formation of
3 functional mammalian myocardium; and
4 comprises a pair of folded polypeptides, the amino acid sequence of each of which
5 comprises a sequence having at least 70% amino acid sequence homology with the C-terminal
6 seven-cysteine domain of human OP-1, mouse OP-1, human OP-2 or mouse OP-2, residues 38-
7 139 of SEQ ID NOs. 5, 6, 7 or 8, respectively.

1 19. A method as in claim 1 wherein said morphogen is selected from the group consisting of
2 OP-1, CBMP-2A (BMP-2), and CBMP-2B (BMP-4).

1 20. A therapeutic composition for promoting the repair or regeneration of mammalian
2 myocardium comprising
3 isolated mammalian myogenic precursor cells, and
4 an amount of a morphogen sufficient to promote proliferation or differentiation of said
5 myogenic precursor cells into functional myocardium in a morphogenically permissive
6 environment.

1 21. A therapeutic composition for promoting the repair or regeneration of mammalian
2 myocardium comprising

3 isolated mammalian myogenic precursor cells, and

4 an amount of an inducer of a morphogen sufficient to promote proliferation or
5 differentiation of said myogenic precursor cells into functional myocardium in a morphogenically
6 permissive environment.

1 22. A therapeutic composition for promoting the repair or regeneration of mammalian
2 myocardium comprising

3 isolated mammalian myogenic precursor cells, and

4 an amount of an agonist of a morphogen receptor sufficient to promote proliferation or
5 differentiation of said myogenic precursor cells into functional myocardium in a morphogenically
6 permissive environment.

1 23. A therapeutic composition for promoting the repair or regeneration of mammalian
2 myocardium comprising

3 isolated mammalian myogenic precursor cells, and

4 an amount of a small molecule morphogenic activator sufficient to promote proliferation
5 or differentiation of said myogenic precursor cells into functional myocardium in a
6 morphogenically permissive environment.

1 24. A method of culturing mammalian myogenic precursor cells comprising
2 isolating said myogenic precursor cells, and
3 culturing said myogenic precursor cells in a medium comprising an amount of a
4 morphogen sufficient to promote proliferation or differentiation of said myogenic precursor cells
5 into functional myocardium in a morphogenically permissive environment.

1 25. A method of culturing mammalian myogenic precursor cells comprising
2 isolating said myogenic precursor cells, and
3 culturing said myogenic precursor cells in a medium comprising an amount of an inducer
4 of a morphogen sufficient to promote proliferation or differentiation of said myogenic precursor
5 cells into functional myocardium in a morphogenically permissive environment.

1 26. A method of culturing mammalian myogenic precursor cells comprising
2 isolating said myogenic precursor cells, and

3 culturing said myogenic precursor cells in a medium comprising an amount of an agonist
4 of a morphogen receptor sufficient to promote proliferation or differentiation of said myogenic
5 precursor cells into functional myocardium in a morphogenically permissive environment.

1 27. A method of culturing mammalian myogenic precursor cells comprising
2 isolating said myogenic precursor cells, and
3 culturing said myogenic precursor cells in a medium comprising an amount of a small
4 molecule morphogenic activator sufficient to promote proliferation or differentiation of said
5 myogenic precursor cells into functional myocardium in a morphogenically permissive
6 environment.

1 28. A method of inducing myogenic precursor cells, naturally competent to differentiate into
2 skeletal or smooth muscle, to differentiate into cardiomyocytes, said method comprising the steps
3 of
4 (a) contacting said myogenic precursor cells with a morphogen; and
5 (b) maintaining the product of (a) in an environment morphogenically permissive for
6 cardiomyogenesis.

1 29. A method of producing replacement cardiomyocytes in a mammal in need thereof, said
2 method comprising the step of implanting into said mammal myogenic precursor cells induced by
3 the method of claim 28.

1 30. A pharmaceutical composition comprising
2 a morphogenic agent selected from the group consisting of a morphogen, a morphogen
3 inducer, an agonist of a morphogen receptor, and a small molecule morphogenic activator; and
4 a mitogen selected from the group consisting of bFGF, IGF, PDGF, LIF, ACTH, MSH,
5 and G-CSF.